

**CELLS HAVING AMPLIFIED SIGNAL TRANSDUCTION PATHWAY
RESPONSES AND USES THEREFOR**

Abstract

The invention provides recombinant cells that have been engineered such that ligand stimulation of a receptor expressed by the cells leads to amplified signal transduction responses. In one embodiment, the receptor-expressing cells have been engineered to carry a heterologous DNA construct comprising a gene encoding a protein that activates the signal transduction pathway, which gene is operatively linked to a promoter that is responsive to activation of the signal transduction pathway. Stimulation of the receptor by a ligand leads to expression of the heterologous DNA construct encoding the protein that activates the signal transduction pathway such that signals generated by ligand binding to the receptor are amplified. Preferred cells are yeast cells expressing heterologous G protein coupled receptors functionally coupled to the yeast pheromone response pathway and overexpressing Ste5p, Ste4p, Ste12p, Ste11p or a dominant truncation allele of Ste20 via a pheromone-responsive promoter. The invention further provides cells expressing a heterologous receptor, wherein an endogenous gene encoding a protein that negatively regulates an endogenous signal transduction pathway is mutated to render the protein nonfunctional such that signals generated by ligand binding to the receptor are amplified. The invention further provides cells expressing a heterologous receptor, wherein an endogenous gene encoding a protein that positively regulates an endogenous signal transduction pathway is mutated to a supersensitive form such that the sensitivity of the pathway to ligand stimulation is increases. Methods of using the cells of the invention to identify receptor modulators are also provided.